PATENT SPECIFICATION 915,066

DRAWINGS ATTACHED.

Date of Application and filing Complete Specification :
Oct. 22, 1959. *No. 35872/59.*

Application made in United States of America (No. 768,979) on Oct. 22, 1958.

Complete Specification Published : Jan. 9, 1963.

Index at Acceptance :—Classes 2(3), H2; and 81(2), Y12.

International Classification :—C08h. A61b.

SPECIFICATION NO. 915,066

By a direction given under Section 17 (1) of the Patents Act 1949 this application proceeded in the name of Ethicon, Inc., a Corporation organised and existing under the laws of the State of New Jersey, United States of America, of U.S. Highway 22, Bridgewater Township, New Jersey, United States of America.

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THE PATENT OFFICE

granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement :—

This invention relates to a dispersion of swollen collagen fibrils in an acid solution and to a process for obtaining such a dispersion. The collagen dispersions of the present invention are useful in the manufacture of absorbable sutures and surgical aids in the form of films, filaments, strands, tubing and sponges. Edible sausage casings have also been made from these collagen dispersions.

For the sake of clarity, the terms used herein are defined as follows :—

The term " native collagen fiber," as used herein, means a thread-like collagen structure as it exists in connective tissue.

The term " swollen collagen fiber," as used herein, means a thread-like collagen structure that has been swollen in a cyanacetic acid solution having a diameter of 200 to 100,000 Angstrom units.

The term " monofilament," as used herein, means a single thread of oriented collagen fibrils as extruded through a single orifice in a spinnerette.

The term " multifilament," as used herein, means a group of individual separate filaments extruded through a spinnerette.

The term " strand," as used herein, means a group of filaments that have been united to form a unitary structure.

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desirable qualities of the fabricated article. Prevention of serious degradation during processing, however, has always been difficult because collagen in the native state is associated with impurities and must be separated therefrom. It has been a disadvantage of the prior art processes for the manufacture of a collagen dispersion that serious denaturation and degradation of the collagen results from the mechanical, thermal and chemical steps employed to separate the collagen from associated non-collagenous impurities.

It is an object of the present invention to separate collagen from connective tissue without changing the original collagen fibril structure.

It is another object of this invention to prepare a homogeneous dispersion of swollen undenatured and undegraded collagen fibrils.

It is also an object of this invention to prepare a dispersion of unprecipitated swollen collagen fibrils that may be extruded into a dehydrating bath to form shaped articles of exceptional strength.

The objects of this invention may be realized by swelling and dispersing collagen fibrils in an aqueous solution of cyanoacetic acid. The aqueous solution of cyanoacetic acid may contain methanol as a cosolvent. One phase of the present invention relates to the observation that collagen fibrils, when swollen in aqueous cyanoacetic acid solution, are not degraded or denatured at temperatures

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COMPLETE SPECIFICATION.

Collagen Article and the Manufacture thereof.

We, HAROLD ROBERT HOCHSTADT, a citizen of the United States of America, of 21 Savage Road, Franklin Park, New Jersey, United States of America, and EMANUEL ROY LIEBERMAN, a citizen of the United States of America, of 119 Branch Road, Somerville, New Jersey, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement :—

This invention relates to a dispersion of swollen collagen fibrils in an acid solution and to a process for obtaining such a dispersion. The collagen dispersions of the present invention are useful in the manufacture of absorbable sutures and surgical aids in the form of films, filaments, strands, tubing and sponges. Edible sausage casings have also been made from these collagen dispersions.

For the sake of clarity, the terms used herein are defined as follows :—

The term " native collagen fiber," as used herein, means a thread-like collagen structure as it exists in connective tissue.

The term " swollen collagen fiber," as used herein, means a thread-like collagen structure that has been swollen in a cyanoacetic acid solution having a diameter of 200 to 100,000 Angstrom units.

The term " monofilament," as used herein, means a single thread of oriented collagen fibrils as extruded through a single orifice in a spinnerette.

The term " multifilament," as used herein, means a group of individual separate filaments extruded through a spinnerette.

The term " strand," as used herein, means a group of filaments that have been united to form a unitary structure.

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The success of a process employing collagen as a basic material is often dependent upon maintaining the collagen fibril structure throughout the process. Denaturation or degradation of the collagen structure prior to or during the casting of a film, spinning of a monofilament, or extrusion of a shaped article, such as a ribbon or a tube, will impair desirable qualities of the fabricated article. Prevention of serious degradation during processing, however, has always been difficult because collagen in the native state is associated with impurities and must be separated therefrom. It has been a disadvantage of the prior art processes for the manufacture of a collagen dispersion that serious denaturation and degradation of the collagen results from the mechanical, thermal and chemical steps employed to separate the collagen from associated non-collagenous impurities.

It is an object of the present invention to separate collagen from connective tissue without changing the original collagen fibril structure.

It is another object of this invention to prepare a homogeneous dispersion of swollen undenatured and undegraded collagen fibrils.

It is also an object of this invention to prepare a dispersion of unprecipitated swollen collagen fibrils that may be extruded into a dehydrating bath to form shaped articles of exceptional strength.

The objects of this invention may be realized by swelling and dispersing collagen fibrils in an aqueous solution of cyanoacetic acid. The aqueous solution of cyanoacetic acid may contain methanol as a cosolvent. One phase of the present invention relates to the observation that collagen fibrils, when swollen in aqueous cyanoacetic acid solution, are not degraded or denatured at temperatures

below about 25° C. Thus, the swollen collagen fibrils may be dehydrated and processed to give multifilaments and strands of exceptional tensile strength.

The invention will appear more clearly from the following detailed description when taken in connection with the accompanying drawings, showing, by way of example, a preferred embodiment of the invention.

Referring now to the drawings :—

Figure 1 is a flow diagram illustrating the sequence of steps in preparing a dispersion of collagen fibrils from animal tendon.

Figure 2 is a drawing of the Superficial Flexor and Deep Flexor Tendons as obtained from cattle and illustrates that portion of the tendon used in preparing the dispersion of the present invention.

Figure 3 is a sectional view of a kettle that is used to prepare a homogeneous dispersion of collagen fibrils and illustrates the associated circulating pump and homogenizing jets.

Figure 4 is a sectional view of the dispersion kettle on the line 4—4 of Figure 3.

Figure 5 is a detailed sectional view of two homogenization jets that are used in the return line to the dispersion kettle.

Figure 6 is an exploded view of a screen filter used to remove non-swollen material from the collagen dispersion.

The general sequence of operations in the formation of a dispersion of pure collagen fibrils is shown by the flow sheet appearing as Figure 1 in the accompanying drawings. By the process to be described, one may disperse the collagen fibrils and remove impurities therefrom without appreciable denaturation or degradation of the collagen structure.

The raw material for the dispersion of this invention is mammalian tendon. Whales are a large source of collagen, and whale tendon is a satisfactory starting material. Pork, sheep and beef tendons are also satisfactory. The best results to date have been obtained using the Deep Flexor Tendon of cattle.

The various sections of bovine tendon are illustrated in Figure 2. In this figure, certain sections of the tendon have been arbitrarily designated by the letters " A," " B," " C " and " D." The " A " portions consist of sheaths (annular ligaments) which surround the two " C " sections. The " A " portions are also connected directly to the " B " tendon. (The Superficial Flexor Tendon.) The " C " material consists of two small dense shanks which branch off the larger " D " section. These " C " portions (branches of the Deep Flexor Tendon) contain a large percentage of material that does not swell in acid solutions. That section of the single shank identified by the letter " D " in Figure 2 (the Deep Flexor Tendon) is the preferred portion of the tendon for preparing the collagen dispersion to be described, but the " B " portion may also be used.

With reference to Figure 1, the beef tendons (preferably Deep Flexor Tendons), as shipped from the packing house and received, are first cleaned of fat, superficial non-collagenous protein, and other extraneous matter. The cleaned tendon is then frozen and then sliced to a thickness of 11 to 25 mils. while in the frozen state. Thicker slices swell slowly in aqueous cyanoacetic acid solutions and are difficult to disperse. Thinner slices disperse readily but the dispersion, when extruded, has poor tensile strength. Preferably, the tendon slices are formed by cutting across the major axis as lengthwise slicing seems to result in a slower swelling. An aliquot sample of the sliced tendon is analyzed at this time for total solids as the moisture contained in the tendon received from various suppliers and at different times is not constant.

The sliced tendon is next treated with an enzyme solution to dissolve the elastin which encircles the native collagen fibers and ties them together. By this treatment substantially all of the elastin is dissolved and can be removed. Proteolytic enzymes from either plant or animal sources may be employed to advantage. Pancreatin is an enzyme that is effective in removing elastin. Enzymes derived from plants, such as ficin, are also useful. Another enzyme that will perform this function is one prepared by extracting commercial malt diastase (U.S.P. IX) with water. The tendon-enzyme mixture is stored at room temperature for 15 to 20 hours.

After the enzyme treatment, which is terminated by the addition of hydrogen peroxide, the tendon slices are washed with water. Soluble proteins and lipids may be removed by treating the slices with a dilute aqueous solution of a chelating agent, such as ethylenediamine tetrasodium tetraacetate. Following this treatment, the tendon slices are washed again to remove residual traces of the chelating agent.

The cleaned tendon slices at this point contain a high percentage of purified collagen associated with material that does not swell in acid solution. The next step is to swell this collagen in a cyanoacetic acid solution to form a homogeneous dispersion of collagen fibrils, but it is most important that during this step the individual slices of collagen be not permitted to coalesce. As collagen swells, it becomes sticky and, if the individual collagen sections are permitted to stick together, the interior of the conglomeration will not have contact with the swelling solution. Therefore, to obtain a homogeneous fiber dispersion in a practical time, it is most desirable to prevent coalescence of the

individual tendon slices. A dispersion kettle (*see* Figures 3 and 4) having a paddle 11 positioned off centre, as shown in the drawings, is used to minimize lump entanglement. In the dispersion kettle, the collagen slices are slowly stirred in the aqueous cyanoacetic acid solution. The collagen slices absorb the cyanoacetic acid solution with swelling.

Temperature becomes a critical factor after addition of acid to the tendon slices as the collagen is degraded in the presence of acids at about 30° C., and above. For this reason, all processing subsequent to the cyanoacetic acid addition should be carried out at temperatures below about 25° C.

The swelling solution is an aqueous solution of cyanoacetic acid containing about 0.25 gram mol. of cyanoacetic acid for each 100 grams (dry weight) of collagen to be treated. Thus an aqueous solution to swell 300 grams of tendon slices (33% solids) may be prepared by dissolving 21.26 grams (0.25 mol.) of cyanoacetic acid in about 10 liters of water. As much as 50 per cent of the water present in the swelling solution may be replaced with methanol. The use of methanol as a cosolvent facilitates the removal of air bubbles from the collagen dispersion. When methanol is used as a cosolvent, however, the amount of cyanoacetic is preferably increased. About twice the quantity of cyanoacetic acid, or 0.50 gram mol. of cyanoacetic acid for each 100 grams (dry weight) of collagen should be used if the aqueous solution contains about 50 per cent methanol. In general, the swelling solution will contain from 0.2 per cent to 0.5 per cent cyanoacetic acid. Less cyanoacetic acid retards swelling and increasing the amount of cyanoacetic acid beyond 0.5 per cent does not appreciably decrease the swelling time or improve the dispersion. The preferred *p*H is 2—3.

It is very difficult to prepare a collagen dispersion containing more than 2 per cent collagen as more concentrated dispersions have an extremely high viscosity. When the collagen dispersion is to be used in spinning processes, the amount of collagen fibers present in the swelling solution is preferably about 1 per cent. A dispersion of collagen fibrils that has a solids content below about 0.8 per cent is difficult to spin. On the other hand, a concentration of collagen fibrils greater than 1 per cent results in a dispersion that is more difficult to extrude. Of equal importance is the difficulty in obtaining and maintaining a homogeneous dispersion when the total solids are too high. It is extremely important that a collagen fibril dispersion which is to be extruded be homogeneous, as a small change in the solids concentration of the material being extruded will result in large cross-sectional variations in the final product.

After most of the swelling has taken place in the dispersion kettle (Figure 3), the dispersion is homogenized by repeated passes through a stainless steel rotary metering pump 12 and stainless steel series-connected jets 13 and 14 having orifices of about 50 mils and 40 mils, respectively. The internal structure of these jets is illustrated by Figure 5. It will be noted from Figure 3 that these jets are positioned in parallel banks. This readily permits isolating any pair of jets from the system for cleaning.

Stirring is continued during homogenization. Best results are obtained with a slow agitation (60 r.p.m.) during the swelling stage, intermittent agitation (60 r.p.m.) at the beginning of homogenization, and higher speed (120 r.p.m.) intermittent agitation near the end of the homogenization.

The homogenizing pump 12 employed in this process is a rotary pump (such as a Zenith pump) that has been modified by milling about 0.003 inch from the circumference of the gear teeth. The intake and exit from the pump are connected to the dispersion kettle by the stainless steel conduit 15 which is capable of withstanding the high pressure.

The homogenizing pump is operated at 190 r.p.m. for two to four hours. The flow rate through the homogenizing jets at the start of this step is irregular and the pressure on the gauge 16 may rise above 200 pounds per square inch. Toward the end of the homogenization step, however, the pressure between the pump and the 50-mil jet 13 is relatively constant at 60 to 80 pounds per square inch.

The dispersion after homogenization still contains fibers of unswollen non-collagenous material which must be removed. This is most readily accomplished by forcing the dispersion under pressure through a leaf filter which retains the unswollen non-collagenous material.

Figure 6 is an exploded view of a leaf filter which may be expanded to include any desired number of screens. A suitable filter may contain three or more screens of No. 316 stainless steel. These screens are separated by $\frac{1}{8}$-inch spacers and decrease in mesh size so that the swollen collagen first passes a 15-mil screen, then a 9-mil screen and finally a 4-mil screen. During the filtration step, the speed of the pump may be varied as necessary to maintain the pressure on the filter below about forty pounds per square inch at all times. Pressures above fifty pounds per square inch may force the non-collagenous impurities into the filtered dispersion.

The dispersion of collagen fibrils after filtration may be deaerated under vacuum and is then ready for storage. If stored at 5° C., or below, the dispersion will remain

substantially unchanged for periods in excess of two or three weeks.

Throughout the Specification and the examples which follow, all quantities are expressed in parts by weight, unless otherwise indicated.

EXAMPLE I.

That portion of the Deep Flexor Tendon of cattle designated in Figure 2 as the " D " section, is cleaned of fat, superficial non-collagenous protein, and other extraneous matter and is sliced on an electric meat-slicing machine (rotary knife) in the frozen condition. The tendon sections are sliced perpendicularly to their longitudinal axis to a thickness of about 11 mils. An aliquot sample of the tendon slices is analyzed; the dry solids amount to 36.97%.

The sliced tendon is next treated with an enzyme solution to dissolve elastin. The enzyme solution is prepared by dissolving 0.15 parts of ficin and 3.75 parts of ethylenediamine tetrasodium tetraacetate in 750 parts of water. Seventy-five parts of the sliced tendon is immersed in this solution which is stored at room temperature overnight. Then, 2.25 parts of 30% hydrogen peroxide is added to destroy any residual ficin.

To this mixture of tendon slices in about 750 parts of water is added an additional 2244 parts of water and 5.87 parts of cyanoacetic acid. The swelling solution is cooled to below 25° C. This mixture is stirred in the dispersion kettle illustrated in Figure 3 at about 60 r.p.m. It is important that the remaining steps in the process be carried out at temperatures below about 25° C., and that the temperature of the collagen dispersion not be allowed to exceed this temperature.

Stirring is continued for about 3 hours, during which time the individual collagen slices are swollen. The dispersion is then homogenized by repeated passes through the stainless steel rotary metering pump 12, as described above, and the stainless steel series-connected jets (13 and 14) having orifices of 50 mils and 40 mils, respectively. During the homogenization, the stirrer in the dispersion kettle is operated intermittently.

The pressure on the high pressure side of the homogenization jets falls to 70 pounds per square inch and remains constant after 3.5 hours, indicating substantially complete homogenization. The dispersion is then forced through a leaf filter containing three screens of No. 316 stainless steel. These screens are separated by $\frac{1}{8}$-inch spacers and decrease in mesh size so that the dispersion first passes a 14-mil screen, then a 9-mil screen, and finally a 4-mil screen. During the filtration step, the pressure on the filter is maintained below about 40 pounds per square inch at all times.

The dispersion of swollen collagen fibrils so obtained analyzes 1.09% solids and has a *p*H of 2.52.

The dispersion may be dehydrated under mild conditions to recover highly purified collagen fibers or may be de-aerated and then extruded through a spinnerette into an acetone dehydrating bath to form collagen filaments, edible sausage casings, and other shaped articles of exceptional strength.

The multifilament so obtained is stretched, twisted, tanned and then again stretched and twisted to coalesce the multifilaments and form a self-bonded unitary strand. The strand, after sterilization, has the following properties :—

Dry straight tensile strength :
2.80 grams per denier.
Dry knot tensile strength :
2.09 grams per denier.
Wet knot tensile strength :
1.81 grams per denier.

The papain digestion time of this strand is 4.1. This is the time in hours required for a 7-inch strand tied to form a loop to go to 20 grams strength at 38° C., in a solution of papain containing 3 grams of the enzyme in 100 milliliters of a buffered solution containing 7.6 grams of thiourea. Four milliliters of 5% sodium cyanide are added to 96 milliliters of the above buffered solution of papain just prior to use.

The hot water digestion time of this strand is 8.9. This is the time, in minutes, required for a 7-inch strand, tied to form a loop, to go to 20 grams strength at 100° C., when immersed in a solution of water buffered at a *p*H of 1.35.

Surgical sponges may be made by freeze drying the collagen dispersion of this example. The collagen dispersion may also be extruded through an annular orifice into a dehydrating bath to form tubular shapes. Such collagen tubes are washed, and tanned to give edible products suitable for sausage casings.

EXAMPLE II.

Fifteen hundred parts of " D " tendon slices, cleaned and sliced as described in Example I to a thickness of 23 mils, are treated with 15,000 parts of an aqueous solution containing 15 parts (0.1%) of ficin, 3.63 parts of disodium ethylenediamine tetraacetic acid and 1.95 parts of ethylenediamine tetrasodium tetraacetic acid. The tendon slices, prior to enzyme treatment, analyze 36.9% solids. After standing for 17 hours at room temperature, the enzyme solution is decanted and a solution containing 50 parts of 30% hydrogen peroxide solution in 15,000 parts of water is added to the slices. The solution is decanted from the tendon slices after 30 minutes and the slices are

rinsed with water. The weight of the water of hydration amounts to 5890.5 parts.

A swelling solution is prepared by adding 235.2 parts (2.76 mols) of cyanoacetic acid to a mixture of 30,473 parts of methanol and 24,576 parts of water and stirring. The enzyme treated slices are added to the acid solution in the dispersion kettle illustrated in Figure 3, and agitated for 1 hour at 60 r.p.m. This dispersion is calculated to contain 0.9% collagen, 0.38% cyanoacetic acid, and equal amounts of water and methanol.

The dispersion is homogenized by repeated passes through a $\frac{1}{2}$-inch pipe. It is then pumped through a $\frac{1}{8}$-inch jet and the dispersion is next circulated through a 60-mil jet for about 15 minutes, finally passing through a leaf filter containing 15-, 9- and 5.5-mil screens.

The deaerated dispersion contains 0.86% solids. This dispersion of swollen collagen fibrils is extruded through a spinnerette into a dehydrating bath. The multifilament so obtained is tanned with chromium, stretched, twisted, washed with water, and then stretched and twisted again to coalesce the multifilament and form a self-bonded unitary strand. The strand (270 denier), after sterilization, has the following properties :—

Dry straight tensile strength :
4.14 grams per denier.
Dry knot tensile strength :
2.09 grams per denier.
Wet knot tensile strength :
1.92 grams per denier.

The papain digestion time is 2.9, and the hot water digestion time is 8.4.

Example III.

Fifteen hundred parts of "D" tendon slices, cleaned and sliced as described in Example I to a thickness of 23 mils are treated with 15,000 parts of an aqueous solution containing 15 parts (0.1%) of ficin, 3.63 parts of disodium ethylenediamine tetraacetic acid and 1.95 parts of ethylenediamine tetrasodium tetraacetic acid. The tendon slices, prior to enzyme treatment, analyze 37.3% solids. After standing for 17 hours at room temperature, the enzyme solution is decanted and a solution containing 50 parts of 30% hydrogen peroxide in 15,000 parts of water is added to the slices. The solution is decanted from the tendon after 30 minutes and the slices are rinsed with water. The weight of the water of hydration amounts to 4040.5 parts.

A swelling solution is prepared by adding 237.8 parts (2.78 mols) of cyanoacetic acid to a mixture of 31,870.3 parts of methanol and 27,929.8 parts of water and stirring. The enzyme treated slices are added to the acid solution in the dispersion kettle illustrated in Figure 3, and the mixture is agitated for 1 hour at 60 r.p.m. This dispersion is calculated to contain 0.87% collagen, 0.37% cyanoacetic acid and equal amounts of water and methanol.

The dispersion is homogenized by repeated passes through a $\frac{1}{2}$-inch pipe. It is then pumped through five $\frac{1}{8}$-inch jets in parallel, the dispersion is next circulated through five 60-mil jets in parallel for about 15 minutes, and is finally filtered through 15-, 9- and 5.5-mil screens.

The dispersion of collagen fibrils so obtained is deaerated, and then extruded through a spinnerette into an acetone dehydrating bath. The multifilament thus produced is tanned with chromium, stretched, twisted, washed with water and then twisted and stretched again. The final product is a dry self-bonded unitary strand (denier 245). This strand, after sterilization, as the following properties :—

Dry straight tensile strength :
4.50 grams per denier.
Dry knot tensile strength :
2.11 grams per denier.
Wet knot tensile strength :
1.96 grams per denier.

The papain digestion time is 2.7, and the hot water digestion time is 8.2.

Example IV.

Twenty-four hundred parts of cleaned tendon as described in Example I sliced to a thickness of 23 mils are treated with 24,000 parts of an aqueous solution containing 24 parts (0.1%) ficin and 9.98 parts (0.001 M.) of ethylenediamine tetrasodium tetraacetate. The tendon slices analyze 37.1% total solids, equivalent to 890.4 parts on a dry weight basis. The *p*H of the enzyme solution is 6.2. After standing for 17 hours at room temperature, the enzyme solution is decanted and the tendon slices are stirred with 24,000 parts of water containing 80 parts of 30% hydrogen peroxide. The hydrogen peroxide solution is drained off and the tendon slices are added to an aqueous methanol solution of cyanoacetic acid made up by adding 51,354.8 parts of methanol and 378 parts of cyanoacetic acid to 49,085.2 parts of water. The amount of cyanoacetic acid in this solution is equivalent to 0.5 mole of acid for each 100 parts of dry solids and the tendon solids amount to 0.86% by weight of the total mixture. The tendon slices are agitated with this acid aqueous methanol mixture for 3 hours at 80 r.p.m. with cooling. The mixture is then circulated through a $\frac{1}{2}$-inch pipe for 1 hour, through $\frac{1}{8}$-inch jets for another hour, and through 60-mil jets for $\frac{1}{2}$-hour. The dispersion is then filtered through a leaf filter

containing 15-, 9- and 5.5-mil screens and deaerated under vacuum. The *p*H of this dispersion is about 2.8.

The dispersion is spun into an acetone dehydrating bath, and the extruded filaments are tanned with a chromium tanning solution, stretched, twisted and tanned with formaldehyde.

Ten feet of the product spun by this method weighs 85 milligrams (250 denier). The strand of this example, when sterilized, has the following physical characteristics :—

Tensile Strength.			Time.	
Dry Straight.	Dry Knot.	Wet Knot.	Papain Digestion.	Hot Water Digestion.
2.20	1.29	1.26	2.4	7.3
2.15	1.27	1.17	2.6	7.3
2.22	1.14	1.23	2.5	7.3
2.26	1.03	1.27		
2.19	1.01	1.31		
2.10	1.14	1.12		
2.07	1.17	1.24		

From the above table, it may be calculated that the average dry straight tensile strength is 2.18 pounds. The average dry knot tensile strength is 1.15 pounds. The average wet knot tensile strength is 1.23 pounds. These values correspond to a dry straight tensile strength of 4.00 grams per denier, a dry knot tensile strength of 2.12 grams per denier, and a wet knot tensile strength of 2.26 grams per denier. The strand of this example is very uniform in diameter, the diameter of 10 random samples being 6.1, 6.5, 6.6, 6.5, 6.6, 6.5, 6.6, 6.5, 6.7, 6.6 mils.

EXAMPLE V.

Twenty-four hundred parts of the tendon described in Example I are sliced to a thickness of 23 mils. This is equivalent to 885.6 parts of tendon solids (36.9%). The tendon slices are treated with 24,000 parts of an aqueous solution containing 24 parts of ficin and 9.98 parts (0.001 M.) of ethylenediamine tetrasodium tetraacetate. The mixture is permitted to stand overnight at 24° C. The enzyme solution is then removed by decantation and the enzyme treated slices are agitated with 24,000 parts of water containing 80 parts of 30% hydrogen peroxide. After ½ hour, the hydrogen peroxide solution is drained from the enzyme treated slices and the slices are added to the solution of cyanoacetic acid containing 376.4 parts of cyanoacetic acid in 48,701.1 parts of water and 51,045.5 parts of methanol. The mixture is agitated for 3 hours at 80 r.p.m. and is then circulated for 1 hour through a ½-inch pipe. The dispersion is circulated for another hour through a ⅛-inch jet and the homogenization is completely accomplished by circulating an additional ½ hour through a 60-mil jet. This dispersion is filtered under pressure of 40 pounds per square inch through a leaf filter containing 15-, 9- and 5.5-mil screens and deaerated under vacuum.

The collagen dispersion (0.86% solids) is aged for 144 hours at room temperature and spun by the process described in the preceding example. The product (250 denier) tested sterile as follows :—

Tensile Strength.			Time.	
Dry Straight.	Dry Knot.	Wet Knot.	Papain Digestion.	Hot Water Digestion.
2.24	1.27	1.00	3.8	6.2
2.42	1.37	1.06	3.8	6.5
2.39	1.37	1.00	3.8	6.0
2.34	1.37	1.17		
2.38	1.14	1.19		
2.37	1.51	1.12		
2.16	1.75	1.06		
	1.78			

From the above table, it may be calculated that the average dry straight tensile strength is 2.33 pounds. The average dry knot tensile strength is 1.48 pounds. The average wet knot tensile strength is 1.09 pounds. These values correspond to a dry straight tensile strength of 4.23 grams per denier, a dry knot tensile strength of 2.68 grams per denier, and a wet knot tensile strength of 1.98 grams per denier. The strand of this example is very

uniform in diameter, the diameter of 10 random samples being 6.2, 6.2, 6.1, 6.4, 6.4, 6.2, 6.3, 6.4, 6.2 and 6.3 mils.

It is an advantage of the dispersion of this invention that even minute air bubbles, which would cause breaks when the dispersion is extruded to form filaments, may be easily removed under vacuum. The aqueous methanol cyanoacetic acid dispersions may be complete deaerated at 15 mm. of mercury within 2 or 3 hours.

WHAT WE CLAIM IS :—

1. A dispersion of swollen undegraded collagen fibers in an aqueous solution containing cyanoacetic acid.

2. A dispersion according to Claim 1 in which the solution contains methanol.

3. A dispersion according to Claim 1 in which the cyanoacetic acid constitutes between 0.2 per cent and 0.5 per cent by weight of the total dispersion.

4. A dispersion according to any of Claims 1—3 in which the collagen content is between 0.8% and 2% by weight.

5. A process for the production of a collagen dispersion capable of extrusion to form a shaped article which comprises swelling and dispersing undegraded collagen fibers in an aqueous solution of cyanoacetic acid.

6. A process according to Claim 5 wherein the solution contains methanol.

7. A process according to any of Claims 5—6 wherein the solution contains between 0.2% and 0.5% cyanoacetic acid.

8. A process according to any of Claims 5—7 wherein the *p*H of the solution is from 2 to 3.

9. A process according to any of Claims 5—8 maintained at a temperature below 25° C.

10. A process according to any of Claims 5—8 wherein the collagen fibers are obtained from animal tendons.

11. A process according to Claim 10 wherein the animal tendons are sliced and then treated with an enzyme composition to isolate the collagen.

12. A process for the production of a collagen dispersion substantially as hereinbefore described with reference to the accompanying drawings.

13. A process for the production of a collagen dispersion substantially as described in any of the foregoing Examples.

14. A dispersion of swollen undegraded collagen fibers whenever produced by a method according to any of Claims 5—13.

15. A method of producing a fabricated collagenous article which comprises extruding a dispersion of collagen fibers according to any of Claims 1—4, or 14.

16. A fabricated collagenous article whenever produced by a method according to Claim 15.

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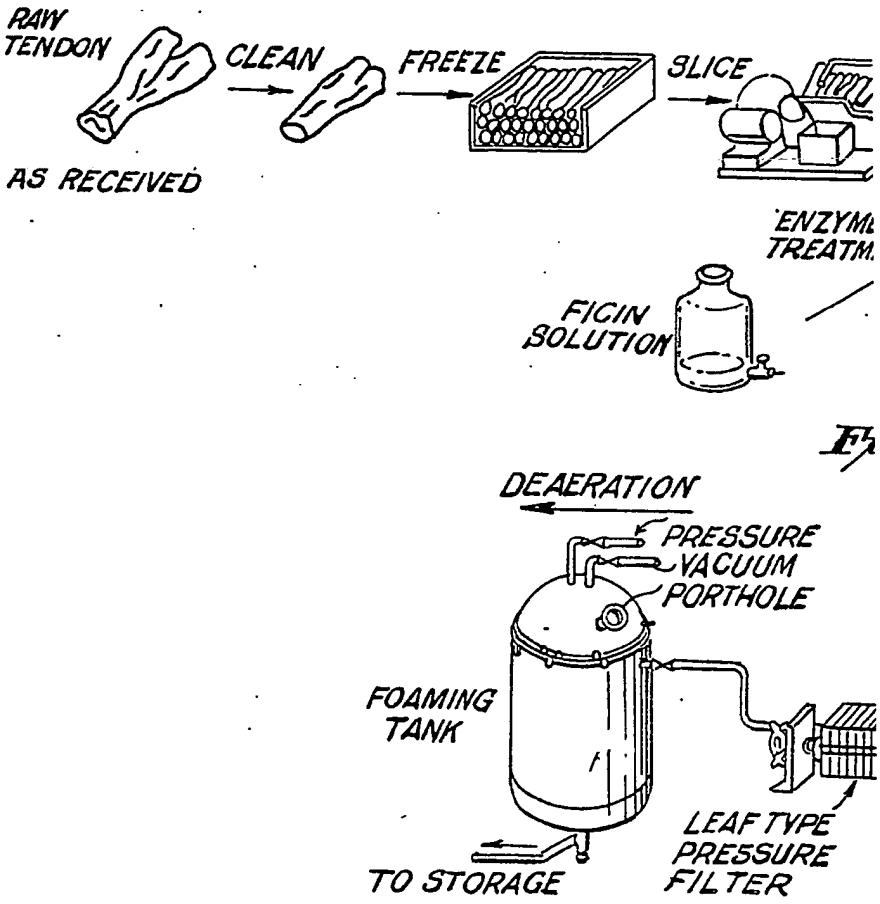
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PORTHOLE
FOAMING TANK
LEAF TYPE PRESSURE FILTER
TO STORAGE

915066 COMPLETE SPECIFICATION
3 SHEETS *This drawing is a reproduction of the Original on a reduced scale*
Sheet 1

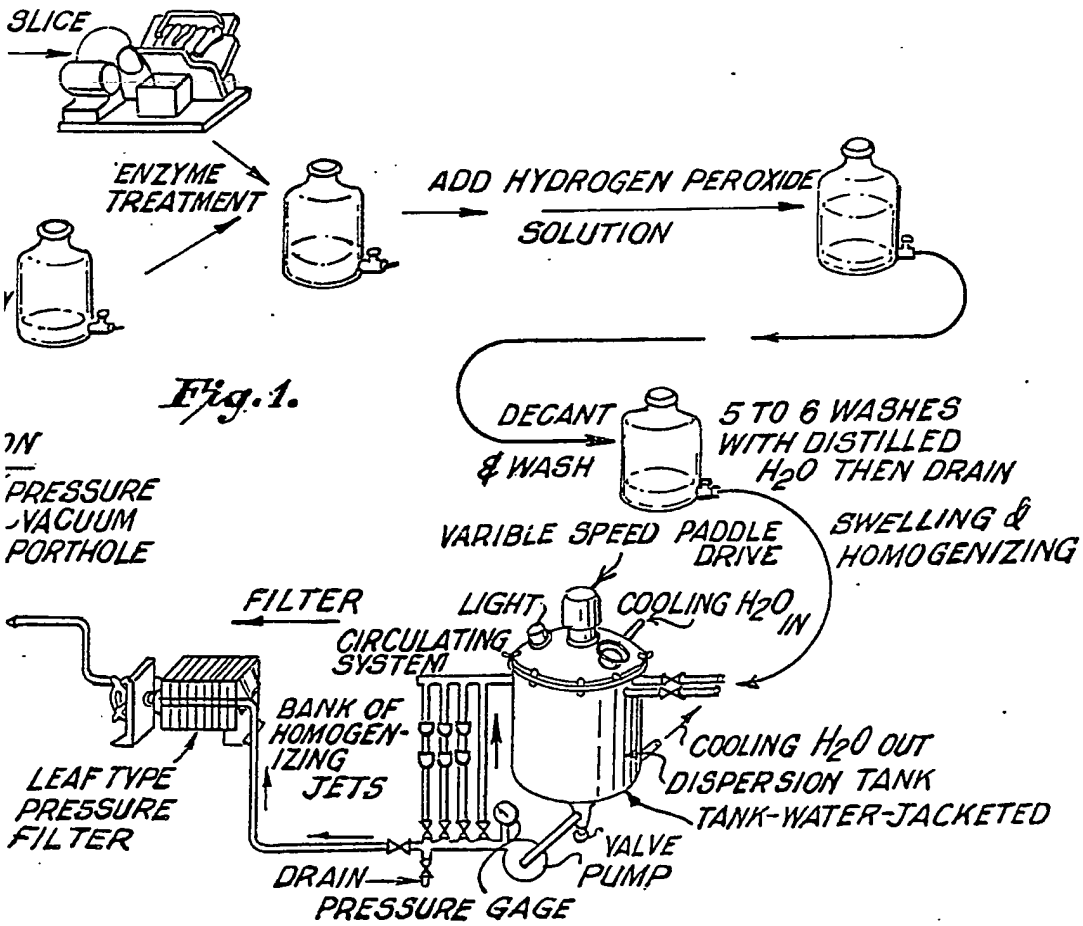

Fig. 1.

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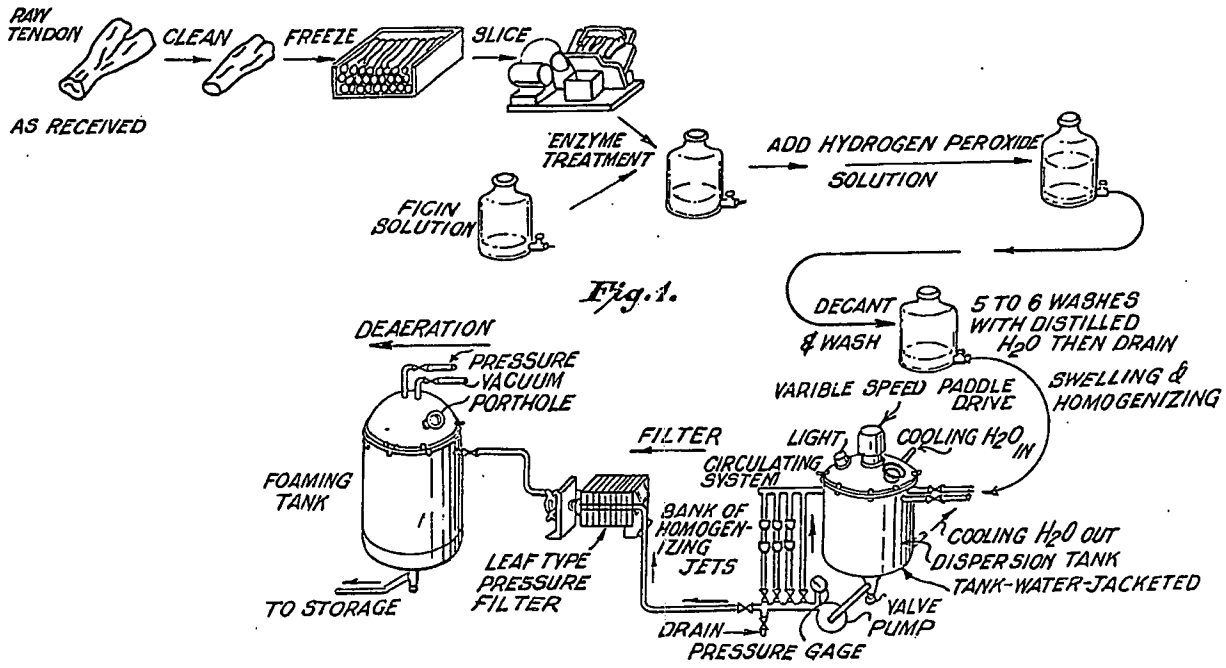
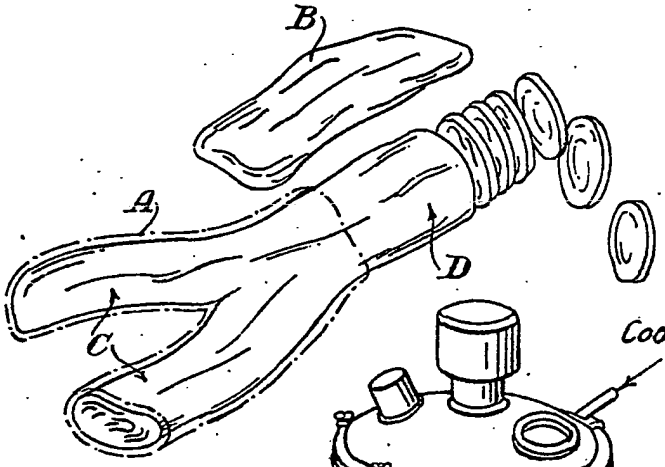


Fig. 1.

Fig. 2.



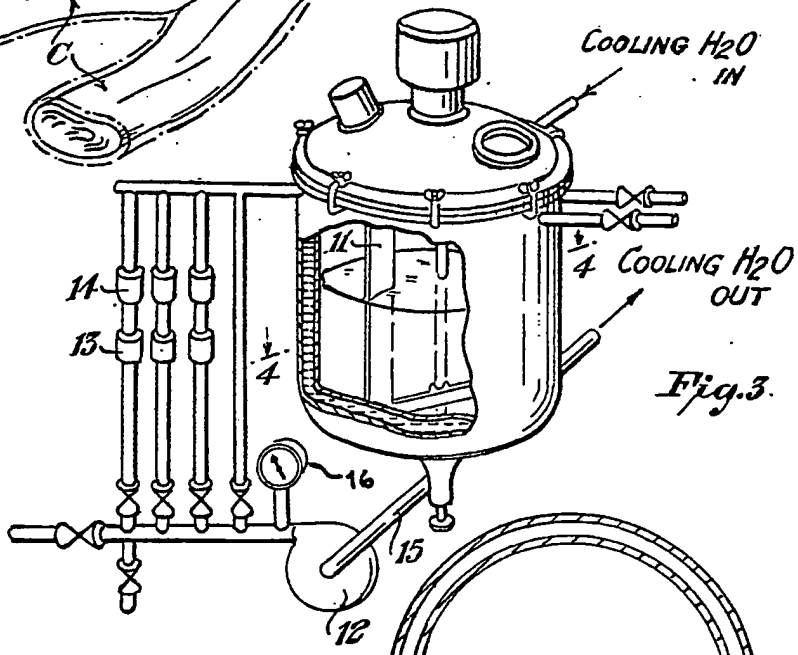


Fig. 3.

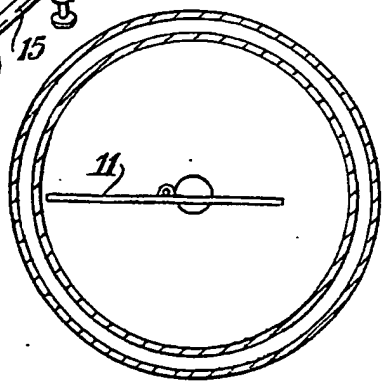


Fig. 4.

915066 COMPLETE SPECIFICATION
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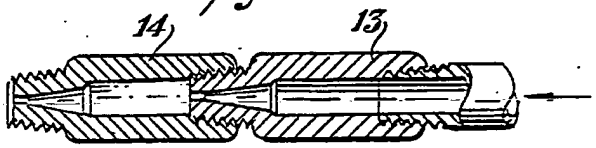
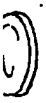
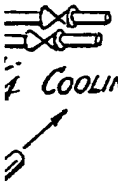
Sheets 2 & 3

Fig.5.





COOLING H_2O IN



COOLING H_2O OUT

Fig.3.

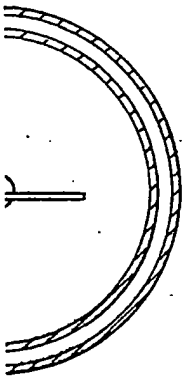
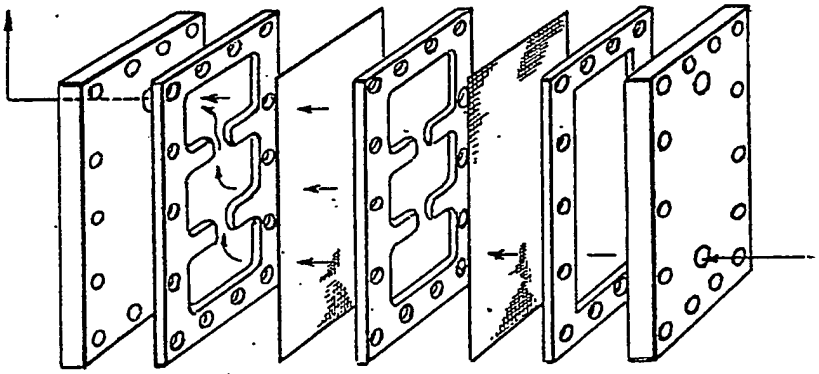


Fig.6.



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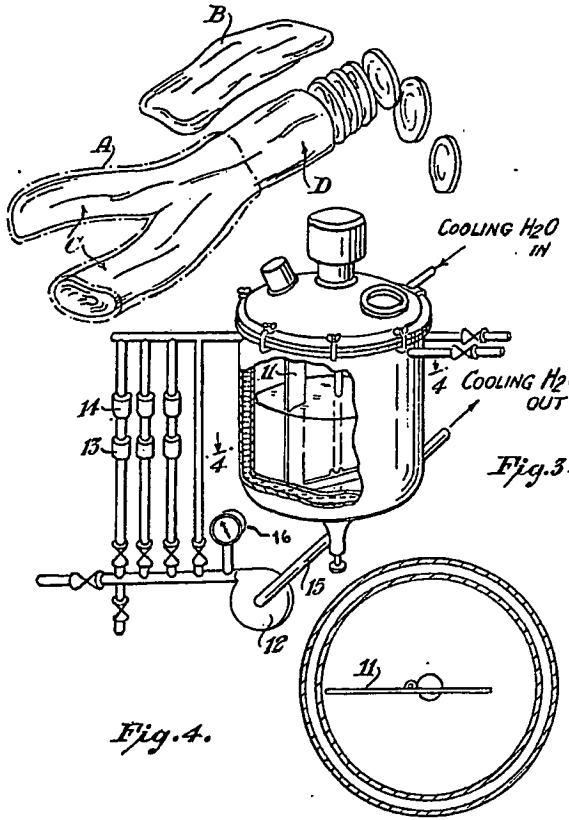

Fig.4.

Fig.3.

Fig.5.

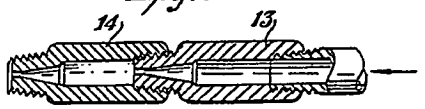

Fig.6.